FILE 'USPAT' ENTERED AT 09:39:20 ON 08 OCT 96

WELCOME TO THE
U.S. PATENT TEXT FILE

=> s (platelet derived growth factor) or pdgf
9551 PLATELET
271215 DERIVED
115401 GROWTH
216248 FACTOR
776 PLATELET DERIVED GROWTH FACTOR
(PLATELET(W)DERIVED(W)GROWTH(W)FACTOR)
591 PDGF
L1 920 (PLATELET DERIVED GROWTH FACTOR) OR PDGF

=> s l1 (w) AA
19549 AA
L2 51 L1 (W) AA

=> d bib date ab 1-

US PAT NO: 5,457,093 [IMAGE AVAILABLE] L2: 17 of 51
DATE ISSUED: Oct. 10, 1995
TITLE: Gel formulations containing growth factors
INVENTOR: John K. Cini, Bethlehem, PA
Amy L. Finkenaur, Neshanic Station, NJ
ASSIGNEE: Ethicon, Inc., Somerville, NJ (U.S. corp.)
APPL-NO: 08/135,230
DATE FILED: Oct. 12, 1993
ART-UNIT: 181
PRIM-EXMR: Howard E. Schain
ASST-EXMR: Sheela J. Huff

L2: 17 of 51
TITLE: Gel formulations containing growth factors
US PAT NO: 5,457,093 DATE ISSUED: Oct. 10, 1995
[IMAGE AVAILABLE]
APPL-NO: 08/135,230 DATE FILED: Oct. 12, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 974,013, Nov. 10, 1992, which is a continuation of Ser. No. 703,584, May 20, 1991, abandoned, which is a continuation of Ser. No. 233,483, Aug. 19, 1988, abandoned, which is a continuation-in-part of Ser. No. 98,816, Sep. 18, 1987, abandoned.

ABSTRACT:
Gel formulations containing polypeptide growth factors having human mitogenic or angiogenic activity are provided. The gel formulations are useful for topical or incisional wound healing for cutaneous wounds, in the anterior chamber of the eye and other ophthalmic wound healing. The gel formulations also comprise a water soluble, pharmaceutically or ophthalmically compatible polymeric material for providing viscosity within various ranges determined by the application of the gel. The gel formulations provide controlled release and increased contact time of the growth factor to the wound site.

US PAT NO: 5,128,321 [IMAGE AVAILABLE] L2: 48 of 51
DATE ISSUED: Jul. 7, 1992
TITLE: PDGF analogs and methods of use
INVENTOR: Mark J. Murray, Seattle, WA
James D. Kelly, Seattle, WA
ASSIGNEE: ZymoGenetics, Inc., Seattle, WA (U.S. corp.)
APPL-NO: 07/230,190
DATE FILED: Aug. 8, 1988
ART-UNIT: 181
PRIM-EXMR: F. T. Moezie
LEGAL-REP: Seed and Berry

L2: 48 of 51
TITLE: PDGF analogs and methods of use
US PAT NO: 5,128,321 DATE ISSUED: Jul. 7, 1992
[IMAGE AVAILABLE] DISCL-DATE: Jul. 18, 2006
APPL-NO: 07/230,190 DATE FILED: Aug. 8, 1988
REL-US-DATA: Continuation-in-part of Ser. No. 896,485, Aug. 13, 1986, Pat. No. 4,766,073, Aug. 23, 1988, which is a continuation-in-part of Ser. No. 705,175, Feb. 25, 1985, Pat. No. 4,801,542, Jan. 31, 1989, which is a continuation-in-part of Ser. No. 660,496, Oct. 12, 1984, Pat. No. 4,769,328, Sep. 6, 1988, which is a continuation-in-part of Ser. No. 941,970, Dec. 15, 1986, Pat. No. 4,849,407, Jul. 18, 1989.

ABSTRACT:

Proteins having substantially the same biological activity as PDGF are provided. In one aspect, a protein homodimer having two polypeptide chains is disclosed, each of the chains being a mosaic of amino acid sequences substantially identical to portions of the A- and B-chains of PDGF, the protein being chemotactic or mitogenic for fibroblasts. Therapeutic compositions comprising such proteins in combination with a physiologically acceptable carrier or diluent are also provided. Such therapeutic compositions may be used within methods for enhancing the wound-healing process in warm-blooded animals.

US PAT NO: 5,094,941 [IMAGE AVAILABLE] L2: 50 of 51
DATE ISSUED: Mar. 10, 1992
TITLE: Monoclonal antibodies to PDGF
INVENTOR: Charles E. Hart, Brier, WA
ASSIGNEE: ZymoGenetics, Inc., Seattle, WA (U.S. corp.)
APPL-NO: 07/139,960
DATE FILED: Dec. 31, 1987
ART-UNIT: 182
PRIM-EXMR: David Saunders
LEGAL-REP: Seed and Berry

L2: 50 of 51
TITLE: Monoclonal antibodies to PDGF
US PAT NO: 5,094,941 DATE ISSUED: Mar. 10, 1992
[IMAGE AVAILABLE]
APPL-NO: 07/139,960 DATE FILED: Dec. 31, 1987

ABSTRACT:
Monoclonal antibodies (MAbs) capable of binding to native PDGF, and MAbs capable of specifically binding to the **PDGF**-**AA**, PDGF-BB and PDGF-AB isoforms are disclosed. The subject MAbs may be used in the detection or purification of native PDGF or selected PGDF isoforms. In addition, the MAbs may be labeled with an imaging agent and used for in vivo diagnostic purposes, or combined with a pharmaceutically acceptable carrier or diluent for use within wound healing compositions.

STN Columbus
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FULL ESTIMATED COST 0.15 0.15

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FILE 'HCAPLUS' ENTERED AT 09:44:34 ON 08 OCT 96
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=> •s (platelet derived growth factor) or pdgf

L1 6183 FILE MEDLINE •
L2 5443 FILE HCAPLUS •

TOTAL FOR ALL FILES•
L3 11626 (PLATELET DERIVED GROWTH FACTOR) OR PDGF

=> •s l3 (w) AA

L4 350 FILE MEDLINE •
L5 347 FILE HCAPLUS •

TOTAL FOR ALL FILES
L6 697 L3 (W) AA•

=> •s l6 and py>1987

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L7 350 FILE MEDLINE •
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L8 347 FILE HCAPLUS •

TOTAL FOR ALL FILES
L9 697 L6 AND PY>1987

=> •s "A chain"

L10 3000 FILE MEDLINE •
•
L11 10789 FILE HCAPLUS •

TOTAL FOR ALL FILES•
L12 13789 "A CHAIN"•

=> •s homodimer#

L13 2231 FILE MEDLINE •
L14 2762 FILE HCAPLUS •
•
TOTAL FOR ALL FILES•
L15 4993 HOMODIMER#•
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=> •s l3 and l12 and l15

L16 43 FILE MEDLINE •
L17 49 FILE HCAPLUS •

TOTAL FOR ALL FILES
L18 92 L3 AND L12 AND L15

=> dup remove l18

PROCESSING COMPLETED FOR L18
L19 56 DUP REMOVE L18 (36 DUPLICATES REMOVED)

=> d bib ab 1-

L19 ANSWER 51 OF 56 MEDLINE DUPLICATE 32
AN 87287282 MEDLINE
TI Possible positive autocrine feedback in the prereplicative phase of human fibroblasts.
AU Paulsson Y; Hammacher A; Heldin C H; Westermark B
SO NATURE, (1987 Aug 20-26) 328 (6132) 715-7.
Journal code: NSC. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8711
AB The growth of normal diploid fibroblasts is generally thought to be tightly controlled by exogenous growth factors such as ***platelet*** - ***derived*** ***growth*** ***factor*** (***PDGF***) and epidermal growth factor (EGF). Subversion of a growth factor pathway at a regulatory point is considered to be a key event in neoplastic transformation and tumorigenesis. Thus, simian sarcoma virus has acquired the gene encoding the B-chain of ***PDGF*** and there is direct experimental proof that SSV-transformation is mediated by a ***PDGF*** -like growth factor. There is accumulating evidence that ***PDGF*** -like molecules are also synthesized and released by certain normal cells, suggesting an important role of cellularly produced ***PDGF*** in development and tissue regeneration. We now present evidence that a transient expression of the gene encoding the ***PDGF*** ***A*** - ***chain*** , and the synthesis and release of functional ***A*** - ***chain*** ***homodimers*** , is an early event in the prereplicative phase of normal human foreskin fibroblasts exposed to ***PDGF*** or EGF. Since these cells are ***PDGF*** -responsive, the results imply the existence of a positive autocrine signal that may serve as an amplifier of the mitogenic response under certain conditions.

L19 ANSWER 52 OF 56 HCAPLUS COPYRIGHT 1996 ACS
AN 1987:489994 HCAPLUS
DN 107:89994
TI Structure and function of ***platelet*** - ***derived*** ***growth*** ***factor***
AU Westermark, Bengt; Heldin, Carl Henrik
CS Dep. Pathol., Univ. Hosp., Uppsala, S-751 85, Swed.
SO Acta Med. Scand., Suppl. (1987), 715, 19-23
CODEN: AMSSAQ; ISSN: 0365-463X
DT Journal; General Review
LA English
AB A review, with 33 refs., on the structure of ***platelet*** - ***derived*** ***growth*** ***factor*** (***PDGF***), the mediation of simian sarcoma virus transformation by a ***PDGF*** -like factor homologous to a B chain ***homodimer*** , the secretion of a ***PDGF*** ***A*** ***chain*** ***homodimer*** by human osteosarcoma, and expression of ***PDGF*** genes and prodn. of ***PDGF*** -like growth factors in normal cells.

L19 ANSWER 53 OF 56 MEDLINE DUPLICATE 33
AN 87125087 MEDLINE
TI Cultured human endothelial cells express ***platelet*** - ***derived*** ***growth*** ***factor*** ***A*** ***chain*** .
AU Collins T; Pober J S; Gimbrone M A Jr; Hammacher A; Betsholtz C; Westermark B; Heldin C H
NC HL-35716
HL-36003
HL-22602
SO AMERICAN JOURNAL OF PATHOLOGY, (1987 Jan) 126 (1) 7-12.
Journal code: 3RS. ISSN: 0002-9440.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8705
AB Four principal cell types involved in the pathophysiologic response of the vessel wall--endothelial cells, smooth muscle cells, platelets, and monocyte/macrophages--secrete ***platelet*** - ***derived*** ***growth*** ***factor*** -like (***PDGF*** -like) mitogenic activities. Extensive structural data on these activities exist only for the mitogen produced by platelets, which is a 30-kd dimeric protein composed of structurally related A and B polypeptide chains encoded by different genes. It was previously demonstrated that normal cultured endothelial cells transcribe mRNA encoding the B chain of ***PDGF*** from the c-sis gene. Here several new structural features of the mitogen produced by cultured vascular endothelial cells are shown. Hybridization analysis of RNA from normal cultured human umbilical vein endothelial (HUVE) cells revealed that they contain three ***PDGF*** ***A*** ***chain*** transcript species. These RNA species comigrated with and appeared to have the same relative abundance as the three RNA species previously identified in RNA from two human tumor cell lines. ***A*** ***chain*** transcripts were not identified in RNA from a strain of bovine aortic endothelial cells or in human dermal fibroblasts. The ***A*** ***chain*** transcripts in HUVE had the same relative abundance as the B chain transcripts. Immunoprecipitation of metabolically labeled endothelial conditioned medium with anti- ***PDGF*** antiserum revealed a 31-kd species which was split by reduction and alkylation into two species of 16.5 and 17 kd. Thus, endothelial cells secrete a dimeric mitogen antigenically related to ***PDGF*** , with a structure identical to previously isolated ***PDGF*** ***A*** - ***chain*** ***homodimer*** . These findings are consistent with the possibility that secretion of ***PDGF*** by human endothelial cells may be regulated independently of B-chain expression.

L19 ANSWER 54 OF 56 MEDLINE DUPLICATE 34
AN 87016914 MEDLINE
TI Human melanoma cell lines of primary and metastatic origin express the genes encoding the chains of ***platelet*** - ***derived*** ***growth*** ***factor*** (***PDGF***) and produce a ***PDGF*** -like growth factor.
AU Westermark B; Johnsson A; Paulsson Y; Betsholtz C; Heldin C H; Herlyn M; Rodeck U; Koprowski H
NC CA-25874
CA-21124
CA-10815
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES
OF AMERICA, (1986 Oct) 83 (19) 7197-200.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8701
AB Normal human melanocytes and five human melanoma cell lines were analyzed for production of ***platelet*** - ***derived*** ***growth*** ***factor*** (***PDGF***)-like activity. Three of the melanoma cell lines released an activity that inhibited binding of 125I-labeled ***PDGF*** to human foreskin fibroblasts and stimulated [3H]thymidine incorporation in such cells. These activities were inhibited by the addition of anti- ***PDGF*** antibodies. All three factor-producing cell lines were derived from the same patient--one originated from the primary tumor (WM 115), and two were from individual lymph-node metastases (WM 239A and WM 266-4). The factor produced by WM 266-4 cells was characterized biochemically in detail. Immunoprecipitated, the metabolically labeled factor migrated in NaDod-SO4/gel electrophoresis as a homogeneous Mr 31,000 species, which under reducing conditions was resolved into two species of Mr 16,500 and Mr 17,000, implying a dimeric structure of the molecule. The factor was purified to homogeneity. Analysis by reverse-phase high-pressure liquid chromatography of reduced and alkylated factor revealed an elution pattern identical to that of ***PDGF*** A chains. Thus, the native molecule appears to be a ***homodimer*** of ***PDGF*** A chains. Blot-hybridization analysis of poly(A)+ RNA from the cell lines with 32P-labeled ***PDGF*** ***A*** ***chain*** and B chain (SIS product) cDNA probes revealed a relative abundance of B chain transcripts in the cell line originating from the primary tumor tissue only but expression of ***A*** ***chain*** in all three cell lines. We conclude that the two structural genes encoding each of the subunit chains of ***PDGF*** can be expressed in human melanoma cells and that the two genes can be independently expressed in such cells.

L19 ANSWER 55 OF 56 MEDLINE DUPLICATE 35
AN 86313671 MEDLINE
TI Rat skeletal myoblasts and arterial smooth muscle cells express the gene for the ***A*** ***chain*** but not the gene for the B chain (c-sis) of ***platelet*** - ***derived*** ***growth*** ***factor*** (***PDGF***) and produce a ***PDGF*** -like protein.
AU Sejersen T; Betsholtz C; Sjolund M; Heldin C H; Westermark B; Thyberg J
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES
OF AMERICA, (1986 Sep) 83 (18) 6844-8.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8612
AB It is shown here that the myogenic cell line L6J1, primary skeletal myoblasts, and primary adult arterial smooth muscle cells express the gene for the ***A*** ***chain*** but not the gene for the B chain (c-sis) of ***platelet*** - ***derived*** ***growth*** ***factor*** (***PDGF***). It is further

demonstrated that conditioned media from L6J1 cultures contain material that (i) competes with 125I-labeled ***PDGF*** for binding to human fibroblasts, (ii) is specifically precipitated by antibodies against ***PDGF*** , and (iii) has a relative molecular mass comparable to that of ***PDGF*** and, after reduction, its constituent subunit chains. The secretion of ***PDGF*** -receptor-competing activity was at a maximum in exponentially growing cultures but remained at a high level also after the cells had become confluent, stopped dividing, and fused to form multinucleate myotubes. Similarly, it was previously demonstrated that adult rat arterial smooth muscle cells in primary culture produce a mitogenic protein with immunological and structural properties similar to ***PDGF*** . In accordance with these findings, it was recently shown that secretion of ***PDGF*** -like mitogens by a number of human tumor cell lines correlates with expression of the gene for the ***A*** ***chain*** rather than the B chain of ***PDGF*** . The results suggest that production of ***homodimers*** of ***PDGF*** A chains may stimulate proliferation of skeletal myoblasts and arterial smooth muscle cells in an autocrine or paracrine manner. This could fulfill important functions during myogenesis in the embryo as well as in tissue repair and atherogenesis in the adult.

L19 ANSWER 56 OF 56 MEDLINE DUPLICATE 36
AN 86118705 MEDLINE
TI A human osteosarcoma cell line secretes a growth factor structurally related to a ***homodimer*** of ***PDGF*** A-chains.
AU Heldin C H; Johnsson A; Wennergren S; Wernstedt C; Betsholtz C; Westermark B
SO NATURE, (1986 Feb 6-12) 319 (6053) 511-4.
Journal code: NSC. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8605
AB ***Platelet*** - ***derived*** ***growth*** ***factor*** (***PDGF***), as purified from fresh human platelets, is a protein of relative molecular mass (Mr) 30,000 composed of two disulphide-linked subunit chains of similar size, named A and B (ref. 1). The dimer structure of PDGRF seems to be important for its biological effects, as reduction irreversibly inactivates the factor; it is not known, however, whether ***PDGF*** exists as a heterodimer or as a mixture of ***homodimers*** . Amino-acid sequence analysis has revealed that the A- and B-chains of human ***PDGF*** are related to each other, and that the B-chain is almost identical to part of the v-sis gene product of simian sarcoma virus (SSV). There is experimental evidence that a ***PDGF*** -like protein is indeed operational in SSV-induced transformation and the biologically active v-sis product is probably structurally similar to a putative dimer of ***PDGF*** B-chains. ***PDGF*** -like growth factors and/or a 4.2-kilobase (kb) c-sis transcript are present in several transformed mammalian cell lines and in certain nontransformed cells; cloned c-sis complementary DNA from human T cells transformed with human T-lymphotropic virus (HTLV) or from human endothelial cells contains the coding sequence for a putative ***PDGF*** B-chain precursor, but apparently lacks ***PDGF*** ***A*** - ***chain*** sequences. We have previously partially purified and characterized a ***PDGF*** -like growth factor from U-2 OS cells (osteosarcoma-derived growth factor, ODGF) and shown that this factor has structural, functional and immunological characteristics in common with ***PDGF*** . We describe here a procedure for the preparation of homogeneous ODGF, and provide evidence that this factor, which binds to the ***PDGF*** receptor, has a structure similar to a ***homodimer*** of ***PDGF*** A-chains.